# The Cardiovascular System in Acute Infectious Disease

**IRVING FINE, M.D., Walnut Creek**

*• Myocarditis may result from a wide variety of acute infectious diseases, but electrocardiographic abnormalities interpreted as indicating myocarditis may arise from a number of other causes.*

*Among the factors which may cause myocarditis are direct invasion by an organism, the toxic products of an organism, hypersensitivity to the products of an organism, drugs used in therapy, deficiency in nutrients, electrolyte imbalance, and, rarely, fever.*

*Recently emphasis has been placed on the finding that circulatory failure in acute infectious diseases is often primarily peripheral, although heart failure due to myocarditis is not uncommon.*

THE TERM "MYOCARDITIS" has been loosely used to denote functional derangement of the myocardium during the course of infectious disease. A number of investigators have made clinical, electrocardiographic and autopsy studies of the heart in a variety of infectious diseases and a high incidence of concomitant "myocarditis" has been reported.[7, 16, 22, 31, 44, 45, 54, 55] The literature contains reports of cardiac abnormalities occurring with diphtheria,[4, 25, 35] scarlet fever and other streptococcal infections,[35, 36, 39, 41] infectious hepatitis,[11] bacterial pneumonia,[10, 24, 46, 63] typhoid fever,[6, 37, 38] gonococcal[53] and meningococcic infections,[30, 47] tuberculosis,[1, 66] typhus,[69] scrub typhus,[29, 50, 58] measles,[9, 21, 43] influenza A infections,[17] mumps,[42, 68] primary atypical pneumonia,[32] infectious mononucleosis,[14] poliomyelitis,[12, 20, 33, 48] and other infectious diseases.

Saphir[44] found evidence of myocarditis in 490 of 5,626 patients that died of a wide variety of infectious disease. Clinical studies have generally indicated a higher percentage of cardiac abnormality. In electrocardiographic studies Burnett and Piltz[7] noted abnormalities in 20 of 55 adults and in 8 of 45 children. Neubauer[31] studied 200 patients with infectious disease and made a diagnosis of myocarditis on clinical observation alone in 55 per cent and on electrocardiographic evidence alone in 24 per cent. Fine, Brainerd, and Sokolow[16] studied 84 patients with a variety of infectious diseases and found clinical and electrocardiographic evidence of myocarditis in about one-third. It is probable that the discrepancy between pathologic and clinical-electrocardiographic evidence of myocarditis arises from the fact that many of the clinical-electrocardiographic abnormalities are due not to true myocarditis but to other pathologic and physiological factors which will be discussed later in this presentation.

Saphir[45] described the heart in myocarditis as characteristically enlarged, with a soft, grayish-yellow myocardium and a few yellowish streaks or minute areas of hemorrhage. Microscopically the process is often patchy, with considerable variation in intensity from one area to another. Muscle necrosis, interstitial edema, and leukocyte infiltration may occur singly or in combination. Saphir emphasized that many sections must be cut and examined before the diagnosis of myocarditis can be excluded. Gore and Saphir[22] reported that of 1,402 instances of myocarditis surveyed at the Army Institute of Pathology, over 90 per cent were non-rheumatic.

Clinical evidence is usually present in myocarditis. The following signs and symptoms justify suspicion: Poor quality of the heart sounds, especially of the mitral first heart sound; a drop in systolic blood pressure of 20 mm. or more; gallop rhythm; pulse rate out of proportion to the fever—either tachycardia or bradycardia; systolic murmur; cardiac enlargement; pallor; cyanosis; vomiting; listlessness; precordial pain; irregularities of rhythm. Saphir[45] stated that myocarditis should be suspected if a patient with an infectious disease suddenly becomes worse without apparent cause.

The electrocardiogram is generally very helpful, especially if unipolar limb and precordial leads are used. The first change is often a broad-topped T wave. This is usually followed in a day or two by diphasic and inverted T waves. The PR interval may become prolonged. More serious conduction defects are not likely to occur except in diphtheritic myocarditis; here they are of grave significance, almost invariably of a fatal condition. RS-T abnormalities are usually minor and not of significance.

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The QT interval may be prolonged. The QRS complex is generally not abnormal.

There are a number of factors that affect cardiac function during infectious disease. In diphtheria the toxin is almost certainly the cause of myocardial damage. This is probably also true of acute streptococcal infections, typhoid fever, bacterial pneumonia and other infections characterized by toxemia. In other diseases the heart may be directly invaded by the infecting organism. In pyemia from various causes, and in acute meningococcemia, metastatic infection of the myocardium has been noted.[44, 47] In benign viral diseases such as mumps, influenza A and infectious mononucleosis it must be postulated that the myocardium is attacked directly by the virus. It has been demonstrated that the virus of encephalomyocarditis directly invades the myocardium.[51]

Hypersensitivity such as occurs in rheumatic fever is a possible cause of myocarditis. Wallgren[66] expressed belief that pericardial effusion in tuberculosis is often due to a tuberculo-allergic reaction. Polyarthritis in gonococcal infections is sometimes a hypersensitivity phenomenon, and myocarditis may be of similar origin in such diseases.

The possible effect of drugs used in therapy must be considered. It has been shown, both clinically and experimentally, that sulfa drugs can cause interstitial myocarditis. They may also cause inflammatory lesions in the peripheral blood vessels indistinguishable from periarteritis nodosa.[19, 56] Emetine when used in the treatment of amebiasis may be cardiotoxic.[27]

Nutritional factors may contribute to myocardial disease. Simonson, Henschel, and Keys[57] reported that electrocardiographic abnormalities developed in a majority of young men undergoing 24 weeks of semi-starvation. Porter and Bloom[37] were of the opinion that heart involvement is not as great a problem in the present-day treatment of typhoid fever because high calorie diets rather than starvation are now used.

Anemia, preexisting or occurring as a result of infectious disease, results in increased work for the heart and in myocardial anoxia. The electrocardiogram may show RS-T and T wave abnormality as a result of anemia.[13]

Thiamine and niacin deficiency may develop during acute infectious disease. Deficiency in either of these vitamins is deleterious to the myocardium and may be reflected in RS-T, T wave, and conduction abnormalities in the electrocardiogram.[15, 67] Rachmilewitz and Braun[38] in a study of typhoid fever found that electrocardiographic abnormalities reverted to normal much faster in a group of patients given 300 to 600 mg. of niacin daily than in a control group.

Electrolyte imbalance frequently occurs during infectious disease. It has been shown that the acidosis and electrolyte imbalance occurring in diabetic coma often result in electrocardiographic abnormalities.[3] Alkalosis has been shown to cause a definite reduction in the amplitude of the T waves, while acidosis causes a striking increase in their height.[2] Hyperpotassemia results in high, peaked T waves, various degrees of heart block, and RS-T elevations.[61] Hypopotassemia results in low or inverted T waves, depression of RS-T, and prolongation of the QT intervals.[40, 60] The characteristic lesions in the heart in experimentally produced potassium deficiency consisted of myocardial and endocardial necrosis with replacement by scar tissue and infiltration by phagocytes.[18]

Reduction of ionized calcium in the serum results in typical changes in the electrocardiogram—prolongation of the QT interval, sharply pointed positive T waves and a long isoelectric course of ST. Dehydration can cause flattening of the T waves and depression of the RS-T segments.[5]

Fever has been thought by some investigators to be the cause of the electrocardiographic abnormalities seen in infectious disease. There have been a number of studies on the effect of fever on the electrocardiogram[8, 16, 26, 28, 52, 64] Most of these studies are in agreement that in only an occasional patient does fever per se cause electrocardiographic abnormality. The tachycardia associated with fever may cause a generalized lowering of the PQRST complex. A patient with poor coronary circulation may have clinical and electrocardiographic evidence of myocardial anoxia owing to the increased work load of the heart. The myocarditis of acute infectious disease generally appears after the patient has been febrile several days, has no relation to the height of the fever, usually persists after the patient is afebrile, and may not appear until that time.

Except in diphtheria, only rarely is there evidence of congestive heart failure if the patient has had no previous cardiac abnormality. There is very little correlation between abnormalities of venous pressure or circulation time and clinical evidence of myocarditis.[16, 55] Saphir, however, concluded from autopsy findings that many deaths occurring during acute infection were directly due to myocarditis, that sudden death due to myocarditis is not uncommon and that clinical signs of heart failure are often present.[46]

Of late the importance of the peripheral circulation in acute infection has received attention. Perry[34] studied the peripheral circulation in lobar pneumonia in adults. He made observations on the color of the skin, on blood pressure, on response of the skin vessels to histamine, to stroking, to epineph-

rine, and to the back-pressure required to obliterate the blanching caused by epinephrine. He noted that the contractile power of the capillaries was impaired and that recovery of the vessels was slow. He concluded that the circulatory failure in pneumonia is really a failure at the periphery. Greene[23] made similar observations on children with pneumonia and concluded that treatment should be directed at the peripheral circulation rather than the heart. Stead and Eket[59] agreed that while many patients with infectious disease die of circulatory failure, the failure is primarily peripheral rather than central. Peripheral circulatory failure may impair the blood supply to the heart and cause ST and T wave abnormalities difficult to distinguish from those of myocarditis.

In the treatment of circulatory failure in acute infection, therefore, it must be borne in mind that the failure is almost always primarily peripheral, resulting in reduction in volume of circulating blood and inadequate venous return. The output of blood is lowered and the venous pressure is decreased. Digitalis is useless in such circumstances and may be harmful, as it will not slow the heart rate and may diminish an already decreased cardiac output. The judicious use of blood and perhaps epinephrine and adrenocortical hormones may be of value.

However, when true heart failure is present, the ordinary measures should be used. Saphir[49] pointed out that the myocarditis of acute infectious disease is generally a very patchy process. Digitalis may be expected to increase the efficiency of the normal heart muscle fibers until the affected ones have recovered. A special problem arises, however, in diphtheria. In patients that have died from diphtheritic myocarditis, generally most of the myocardium is quite necrotic. The clinical experience has been that digitalis is of little value in the treatment of myocardial failure due to diphtheria, but there is little to lose in a trial of digitalis, since severe diphtheritic myocarditis is almost invariably fatal.

Acute heart failure sometimes develops in babies with bronchiolitis. The babies are generally not in a toxic state but have pronounced respiratory distress because of obstruction of the terminal bronchioles. It has been the observation of many pediatricians that digitalis may be life-saving when cardiac dilation, extreme tachycardia, hepatomegaly and other signs of heart failure develop. It may be postulated that the acute emphysema secondary to terminal bronchiole obstruction causes reduction in the capacity of the pulmonary vascular bed, which results in pulmonary hypertension. In addition the anoxia present causes an increase in pulmonary artery pressure. Anoxia also increases the work and decreases the efficiency of the heart. These factors result in acute dilation of the right ventricle which may develop into cardiac decompensation. Rarely, pertussis may cause a similar problem of cor pulmonale.[62, 65]

1885 Oak Park Boulevard.

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